

## SEARCH REQUEST FORM

## Scientific and Technical Information Center

Requester's Full Name: J. SETHARASGYAN Examiner #: 78224 Date: 7/3/01  
 Art Unit: 1647 Phone Number 305-1117 Serial Number: 091454223  
 Mail Box and Bldg/Room Location: 10016 Results Format Preferred (circle): PAPER DISK E-MAIL  
Box 10C01

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Multimeric forms of the TNF Superfamily ligands

Inventors (please provide full names): Richard Kornbluth

Earliest Priority Filing Date: 12/09/99

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Describes tumor necrosis factor superfamily (TNFSF)  
 fusion proteins specifically CD40L (CD154).

POINT OF CONTACT:  
 BARB O'BRYEN  
 TECH. INFORMATION SPECIALIST  
 STIC CM1 12C14 308-4291

\*\*\*\*\*  
 STAFF USE ONLY  
 Searcher: 1-22  
 Searcher Phone #:   
 Searcher Location:   
 Date Searcher Picked Up:   
 Date Completed: 7-27-01  
 Searcher Prep & Review Time: 25  
 Clerical Prep Time:   
 Online Time: 37

Type of Search	Vendors and cost where applicable
NA Sequence (#)	STN <u>162</u>
AA Sequence (#)	Dialog <u></u>
Structure (#)	Questel/Orbit <u></u>
Bibliographic <u>X</u>	Dr. Link <u></u>
Litigation	Lexis/Nexis <u></u>
Fulltext	Sequence Systems <u></u>
Patent Family	WWW/Internet <u></u>
Other	Other (specify) <u></u>

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=> fil cap1; d que 117; fil wpids; d que 126; fil biotechno; d que 133; fil med1; d que 153; fil embase; d que 161

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FILE COVERS 1947 - 20 Jul 2001 VOL 135 ISS 5

FILE LAST UPDATED: 19 Jul 2001 (20010719/ED)

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L4	81	SEA FILE=CAPLUS ABB=ON	(TNF OR TUMOR NECROSIS FACTOR) (W) (SUPER FAMILY OR SUPER FAMILY)
L5	10257	SEA FILE=CAPLUS ABB=ON	TUMOR NECROSIS FACTORS+NT/CT
L6	33094	SEA FILE=CAPLUS ABB=ON	TUMOR NECROSIS FACTORS+OLD/CT
L7	24912	SEA FILE=CAPLUS ABB=ON	COLLECTIN#
L8	1981	SEA FILE=CAPLUS ABB=ON	SPD OR (SURFACTANT PROTEIN OR SP) (W) D
L9	847	SEA FILE=CAPLUS ABB=ON	"SURFACTANT PROTEINS (PULMONARY)"+OLD/C T
L10	17	SEA FILE=CAPLUS ABB=ON	TNFSF##
L11	3613	SEA FILE=CAPLUS ABB=ON	CD40# OR CD154 OR (CD(W) (40# OR 154))
L12	1027	SEA FILE=CAPLUS ABB=ON	LTA
L14	247	SEA FILE=CAPLUS ABB=ON	LTB
L15	120289	SEA FILE=CAPLUS ABB=ON	FUSION/OBI
L16	61469	SEA FILE=CAPLUS ABB=ON	MULTIMER? OR TRIMER? OR CHIMER? OR CHIMAER?
L17	7	SEA FILE=CAPLUS ABB=ON	((L4 OR L5 OR L6) OR (L10 OR L11 OR L12) OR L14) AND ((L7 OR L8 OR L9)) AND (L15 OR L16)

FILE 'WPIDS' ENTERED AT 10:25:37 ON 20 JUL 2001

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FILE LAST UPDATED: 19 JUL 2001

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200140 &lt;200140/DW&gt;

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SEE <http://www.derwent.com/covcodes.html> <<<

L19	2 SEA FILE=WPIDS ABB=ON TNFSF#
L20	2875 SEA FILE=WPIDS ABB=ON (TUMOR OR TUMOUR) (W) NECROSIS (W) FACTOR#
L21	OR TNF
L22	100 SEA FILE=WPIDS ABB=ON LTA OR LTB OR (LYMPHOTOXIN# OR LYMPHO-
L23	TOXIN#) (W) (ALPHA OR BETA)
L24	237 SEA FILE=WPIDS ABB=ON CD40# OR CD154 OR CD(W) (40# OR 154)
L25	60964 SEA FILE=WPIDS ABB=ON COLLECTIN# OR SPD
L26	58 SEA FILE=WPIDS ABB=ON (SP OR SURFACTANT PROTEIN#) (A) (D OR
	PULMONARY)
	7432 SEA FILE=WPIDS ABB=ON MULTIMER? OR TRIMER? OR CHIMER? OR
	CHIMAER?
	2 SEA FILE=WPIDS ABB=ON ((L19 OR L20 OR L21 OR L22)) AND (L24
	OR L23) AND L25

[FILE 'BIOTECHNO'] ENTERED AT 10:25:38 ON 20 JUL 2001

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FILE LAST UPDATED: 17 JUL 2001 <20010717/UP>  
FILE COVERS 1980 TO DATE.>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN  
/CT AND BASIC INDEX <<<

L27	25123 SEA FILE=BIOTECHNO ABB=ON (TUMOR OR TUMOUR) (W) NECROSIS (W) FACTO
L28	R# OR TNF OR TNFSF#
L29	1548 SEA FILE=BIOTECHNO ABB=ON LTA OR LTB OR (LYMPHOTOXIN# OR
L30	LYMPHO TOXIN#) (W) (ALPHA OR BETA)
L31	2037 SEA FILE=BIOTECHNO ABB=ON CD40# OR CD154 OR CD(W) (40# OR 154)
L32	2049 SEA FILE=BIOTECHNO ABB=ON COLLECTIN# OR SPD
L33	280 SEA FILE=BIOTECHNO ABB=ON (SP OR SURFACTANT PROTEIN#) (A) (D OR
	PULMONARY)
	20801 SEA FILE=BIOTECHNO ABB=ON MULTIMER? OR TRIMER? OR CHIMER? OR
	CHIMAER?
	0 SEA FILE=BIOTECHNO ABB=ON (L27 OR L28 OR L29) AND (L30 OR
	L31) AND L32

FILE 'MEDLINE' ENTERED AT 10:25:40 ON 20 JUL 2001

FILE LAST UPDATED: 16 JUL 2001 (20010716/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

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THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

L41	33187	SEA FILE=MEDLINE ABB=ON	TUMOR NECROSIS FACTOR/CT OR TNFSF##
L42	1781	SEA FILE=MEDLINE ABB=ON	LYMPHOTOXIN/CT
L43	1758	SEA FILE=MEDLINE ABB=ON	ANTIGENS, CD40/CT
L44	1233	SEA FILE=MEDLINE ABB=ON	CD40 LIGAND/CT
L46	810	SEA FILE=MEDLINE ABB=ON	SPD OR (SP OR SURFACTANT OR LUNG OR PULMONARY) (1W) (PROTEIN# OR GLYCOPROTEIN#) (W)D
L47	409	SEA FILE=MEDLINE ABB=ON	SURFACTANT PROTEIN# (2A) (PULMONARY OR LUNG)
L48	134585	SEA FILE=MEDLINE ABB=ON	RECOMBINANT PROTEINS+NT/CT
L50	117864	SEA FILE=MEDLINE ABB=ON	FUSION OR MULTIMER? OR TRIMER? OR CHIMER? OR CHIMAER?
L52	3346	SEA FILE=MEDLINE ABB=ON	CD40# OR CD154 OR CD(W) (40# OR 154)
L53	0	SEA FILE=MEDLINE ABB=ON	((L41 OR L42 OR L43 OR L44) OR L52) (AND (L46 OR L47) AND (L48 OR L50))

FILE 'EMBASE' ENTERED AT 10:25:40 ON 20 JUL 2001

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FILE COVERS 1974 TO 19 Jul 2001 (20010719/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L54	12263	SEA FILE=EMBASE ABB=ON	TUMOR NECROSIS FACTOR/CT
L55	2071	SEA FILE=EMBASE ABB=ON	LYMPHOTOXIN/CT
L56	675	SEA FILE=EMBASE ABB=ON	SURFACTANT PROTEIN D/CT OR SPD
L57	11405	SEA FILE=EMBASE ABB=ON	COLLECTIN#
L58	9	SEA FILE=EMBASE ABB=ON	TNFSF##
L59	3286	SEA FILE=EMBASE ABB=ON	CD40# OR CD154 OR CD(W) (40# OR 154)
L60	81673	SEA FILE=EMBASE ABB=ON	FUSION OR MULTIMER? OR TRIMER? OR CHIMER? OR CHIMAER?
L61	0	SEA FILE=EMBASE ABB=ON	((L54 OR L55 OR L58 OR L59) AND L60 AND (L56 OR L57))

=> fil CABAB, JICST-EPLUS, BIOSIS, CONFSCI, BIOTECHDS  
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=> d que 140

L34 79420 SEA (TUMOR OR TUMOUR) (W) NECROSIS(W) FACTOR# OR TNF OR TNFSF#  
 L35 3121 SEA LTA OR LTB OR (LYMPHOTOXIN# OR LYMPHO TOXIN#) (W) (ALPHA OR  
 BETA)  
 L36 4810 SEA CD40# OR CD154 OR CD(W) (40# OR 154)  
 L37 35467 SEA COLLECTIN# OR SPD  
 L38 1540 SEA (SP OR SURFACTANT PROTEIN#) (A) (D OR PULMONARY)  
 L39 57386 SEA MULTIMER? OR TRIMER? OR CHIMER? OR CHIMAER?  
 L40 1 SEA (L34 OR L35 OR L36) AND (L37 OR L38) AND L39

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 PROCESSING COMPLETED FOR L40  
 PROCESSING COMPLETED FOR L26

L63 9 DUP REM L17 L40 L26 (1 DUPLICATE REMOVED)  
 ANSWERS '1-7' FROM FILE CAPLUS  
 ANSWER '8' FROM FILE BIOSIS  
 ANSWER '9' FROM FILE WPIDS

=> d ibib ab 1-9; fil hom

L63 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1  
 ACCESSION NUMBER: 2001:435124 CAPLUS  
 DOCUMENT NUMBER: 135:45182  
 TITLE: Multimeric forms of TNF  
 superfamily ligands  
 INVENTOR(S): Kornbluth, Richard S.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 73 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042298	A1	20010614	WO 2000-US7380	20000320
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1999-454223 A 19991209

AB A method for constructing stable bioactive fusion proteins of the difficult to express tumor necrosis factor superfamily (TNFSF), and particularly members CD40L (CD154) and RANKL/TRANCE, with collectins, particularly pulmonary surfactant protein D (SPD) is described. Single trimers of these proteins lack the full stimulatory efficacy of the natural membrane forms of these proteins in many cases. The multimeric nature of these sol. fusion proteins enables them to engage multiple receptors on the responding cells, thereby, mimicking the effects of the membrane forms of these ligands. For CD40L-SPD, the resulting protein stimulates B cells, macrophages, and dendritic cells, indicating its potential usefulness as a vaccine adjuvant. The large size of these fusion proteins makes them less likely to diffuse into the circulation, thereby limiting their potential systemic toxicity. This property may be esp. useful when these proteins are injected locally as a vaccine adjuvant or tumor immunotherapy agent to prevent them from diffusing away. In addn., these and other TNFSF-collecting fusion proteins present new possibilities for the expression of highly active, multimeric, sol. TNFSF members.

REFERENCE COUNT: 2

REFERENCE(S):  
 (1) Gires, O; EMBO J 1999, V16(20), P6131  
 (2) Pison, U; Eur J Clin Inv 1994, V24(9), P586 CAPLUS

L63 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:168035 CAPLUS

DOCUMENT NUMBER: 134:236228

TITLE: CD40 ligand and CD40 agonist compositions and methods of use

INVENTOR(S): Ahuja, Seema S.; Bonewald, Lynda F.

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: PCT Int. Appl., 117 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016180	A2	20010308	WO 2000-US23276	20000824
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-151250 P 19990827

AB Disclosed are uses of compns. contg. one or more CD40 agonists,

such as CD40 ligands and/or agonistic anti-CD40 antibodies, to reduce or prevent cell death, or apoptosis, in bone cells. Methods of treating or preventing bone loss, including osteoporosis, as well as methods of reducing or eliminating the bone loss assocd. with steroid administration are also provided. Further provided are a variety of therapeutic kits and cocktails.

L63 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 2000:392367 CAPLUS  
 DOCUMENT NUMBER: 133:133979  
 TITLE: Human SP-A protein variants derived from one or both genes stimulate TNF-.alpha. production in the THP-1 cell line  
 AUTHOR(S): Wang, Guirong; Phelps, David S.; Umstead, Todd M.;  
 CORPORATE SOURCE: Floros, Joanna  
 Departments of Cellular and Molecular Physiology, The Pennsylvania State University College of Medicine, Hershey, PA, 17033, USA  
 SOURCE: Am. J. Physiol. (2000), 278(5, Pt. 1), L946-L954  
 PUBLISHER: CODEN: AJPHAP; ISSN: 0002-9513  
 DOCUMENT TYPE: American Physiological Society  
 LANGUAGE: Journal  
 English  
 AB In humans, 2 functional genes of surfactant protein (SP) A, SP-A1 and SP-A2, and several alleles of each functional gene have been characterized. SP-A is a **multimeric** mol. consisting of 6 **trimers**. Each **trimer** contains 2 SP-A1 mols. and 1 SP-A2 mol. Until now, it has been unclear whether a single SP-A gene product is functional or whether there are functional differences either among alleles or between single-gene SP-A products and SP-A products derived from both genes. The authors tested the ability of in vitro expressed SP-A variants to stimulate tumor necrosis factor (TNF)-.alpha. prodn. by THP-1 cells. They obsd. that (1) single-gene products and products derived from both genes stimulate TNF-.alpha. prodn., (2) there are differences among SP-A1 and SP-A2 alleles in their ability to stimulate TNF-.alpha. prodn., and (3) the increases in TNF-.alpha. prodn. are lower after treatment with the SP-A1 alleles than after treatment with the SP-A2 alleles. Furthermore, coexpressed SP-As from SP-A1 and SP-A2 genes have a higher activity compared with SP-As from individual alleles or mixed SP-As from SP-A1 and SP-A2 genes. Thus, the SP-A-induced increases in TNF-.alpha. levels differ among SP-A variants and appear to be affected by SP-A genotype and whether SP-A is derived from one or both genes.

REFERENCE COUNT: 43  
 REFERENCE(S):

- (1) Batenburg, J; Prog Lipid Res 1998, V37, P235 CAPLUS
- (2) Benne, C; J Infect Dis 1995, V171, P335 CAPLUS
- (4) Crouch, E; Am J Respir Cell Mol Biol 1998, V19, P177 CAPLUS
- (5) Elhalwagi, B; Biochemistry 1997, V36, P7018 CAPLUS
- (6) Floros, J; Am J Respir Cell Mol Biol 1996, V15, P489 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L63 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:795994 CAPLUS  
 DOCUMENT NUMBER: 132:31744  
 TITLE:

INVENTOR(S): Gene probes used for genetic profiling in healthcare screening and planning  
 PATENT ASSIGNEE(S): Roberts, Gareth Wyn  
 SOURCE: Genostic Pharma Ltd., UK  
 PCT Int. Appl., 745 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:	DATE
GB 1998-12099	A 19980606
GB 1998-13291	A 19980620
GB 1998-13611	A 19980624
GB 1998-13835	A 19980627
GB 1998-14110	A 19980701
GB 1998-14580	A 19980707
GB 1998-15438	A 19980716
GB 1998-15574	A 19980718
GB 1998-15576	A 19980718
GB 1998-16085	A 19980724
GB 1998-16086	A 19980724
GB 1998-16921	A 19980805
GB 1998-17097	A 19980807
GB 1998-17200	A 19980808
GB 1998-17632	A 19980814
GB 1998-17943	A 19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education

services and social services.

L63 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:795993 CAPLUS  
 DOCUMENT NUMBER: 132:31743  
 TITLE: Gene probes used for genetic profiling in healthcare screening and planning  
 INVENTOR(S): Roberts, Gareth Wyn  
 PATENT ASSIGNEE(S): Genostic Pharma Limited, UK  
 SOURCE: PCT Int. Appl., 149 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

GB 1998-12098	A	19980606
GB 1998-28289	A	19981223
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819
WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L63 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1994:575846 CAPLUS  
 DOCUMENT NUMBER: 121:175846  
 TITLE: 3'-Untranslated region of SP-B mRNA mediates inhibitory effects of TPA and TNF-.alpha. on SP-B expression  
 AUTHOR(S): Pryhuber, Gloria S.; Church, Susan L.; Kroft, Tim;  
 Panchal, Asha; Whitsett, Jeffrey A.  
 CORPORATE SOURCE: Med. Cent., Children's Hosp., Cincinnati, OH,  
 45229-3039, USA  
 SOURCE: Am. J. Physiol. (1994), 267(1, Pt. 1), L16-L24  
 CODEN: AJPHAP; ISSN: 0002-9513  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Surfactant protein-B (SP-B) is a small hydrophobic polypeptide that enhances spreading and stability of surfactant phospholipids in the alveolus of the lung. Decreased expression of SP-B is assocd. with respiratory failure in premature infants and in adult patients with acute respiratory distress syndrome (ARDS). Tumor necrosis factor-.alpha. (TNF-.alpha.) and 12-O-tetradecanoylphorbol-13 acetate (TPA) cause ARDS-like lung injury in vivo. Inhibitory effects of TPA and TNF-a on SP-B mRNA expression in vitro were mediated by decreased SP-B mRNA stability rather than by decreased rate of SP-B gene transcription. In the present study, a human pulmonary adenocarcinoma cell line, NCI H441-4, was stably transfected with expression vectors consisting of the thymidine kinase (TK) promotor and human growth hormone (hGH) gene, in which the hGH 3'-untranslated region (3'-UTR) was replaced by the 2.0-kb human SP-B cDNA [pTKGH(SP-B2.0)] or the 837-bp human SP-B 3'-UTR [pTKGH(SP-B.837)]. The mRNAs and cellular growth hormone protein generated from the chimeric TKGH(SP-B2.0) and TKGH(SP-B.837) genes were each inhibited by .apprx.50% by TPA and TNF-.alpha.. Dexamethasone decreased the inhibitory effects of TPA and TNF-.alpha.. The inhibition of steady-state hGH-SP-B mRNA by TPA and TNF-a was mediated by a cis-active element located in the 3'-UTR region of SP-B mRNA.

L63 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1993:118249 CAPLUS  
 DOCUMENT NUMBER: 118:118249  
 TITLE: Enrichment method for variant proteins with altered binding properties  
 INVENTOR(S): Garrard, Lisa J.; Henner, Dennis J.; Bass, Steven;  
 Greene, Roland; Lowman, Henry B.; Wells, James A.;  
 Matthews, David J.  
 PATENT ASSIGNEE(S): Genentech, Inc., USA  
 SOURCE: PCT Int. Appl., 101 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9209690	A2	19920611	WO 1991-US9133	19911203
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2095633	AA	19920604	CA 1991-2095633	19911203
EP 564531	A1	19931013	EP 1992-902109	19911203
EP 564531	B1	19980325		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 07503600	T2	19950420	JP 1991-502710	19911203

AT 164395	E 19980415	AT 1992-902109	19911203
ES 2113940	T3 19980516	ES 1992-902109	19911203
US 5750373	A 19980512	US 1993-50058	19930430
US 5688666	A 19971118	US 1994-182530	19940114
US 5780279	A 19980714	US 1995-418928	19950405
US 5846765	A 19981208	US 1995-441871	19950516
US 6040136	A 20000321	US 1997-923854	19970903
PRIORITY APPLN. INFO.:			
		US 1990-621667	A 19901203
		US 1991-683400	A 19910410
		US 1991-715300	A 19910614
		US 1991-743614	A 19910808
		US 1988-264611	B2 19881028
		US 1991-682400	B2 19910410
		WO 1991-US9133	W 19911203
		US 1992-864452	B1 19920419
		US 1993-50058	A2 19930430
		US 1993-161692	A1 19931203
		US 1995-418928	A3 19950405
		US 1995-463587	A3 19950605

AB A method for selecting variants of proteins such as growth hormone and antibody fragment with altered binding properties for their resp. receptor mols. is provided. The method comprises fusing a gene encoding a protein of interest to at least a portion of the gene for a phage coat protein, e.g. for the C-terminal domain of the gene III coat protein of M13 under control of a transcription-regulating element. The vector is mutated at .gtoreq.1 position within the 1st gene (e.g. by oligonucleotide-directed mutagenesis), and host cells are transformed with the mutant vector and a helper phage having the coat protein gene. Recombinant phagemid particles are formed contg. at least part of the mutant expression vector and capable of transforming the host; conditions are adjusted so that most phagemid particles do not display >1 copy of the fusion protein on the particle surface. The phagemid particles are screened for binding to the target mol. These steps may be repeated. Phagemids presenting human growth hormone (hGH)-gene III protein fusion proteins prep'd. as above were fractionated chromatog. on immobilized hGH-binding protein; a single cycle of binding and elution gave >5000-fold enrichment.

L63 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS  
 ACCESSION NUMBER: 2001:39801 BIOSIS  
 DOCUMENT NUMBER: PREV200100039801  
 TITLE: CD40L (CD154) fusion protein with  
 pulmonary surfactant protein  
 D as a prototype for soluble multimeric  
 TNF superfamily ligand molecules.  
 Kornbluth, R. S. (1); Kee, K. (1); Truong, N. H. (1)  
 (1) University of California San Diego and VA San Diego  
 Healthcare System, La Jolla, CA USA  
 FASEB Journal, (April 20, 2000) Vol. 14, No. 6, pp. A1162.

AUTHOR(S):  
 CORPORATE SOURCE:  
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 Meeting Info.: Joint Annual Meeting of the American  
 Association of Immunologists and the Clinical Immunology  
 Society Seattle, Washington, USA May 12-16, 2000  
 ISSN: 0892-6638.

DOCUMENT TYPE:  
 LANGUAGE:  
 SUMMARY LANGUAGE:

L63 ANSWER 9 OF 9 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 ACCESSION NUMBER: 1989-154899 [21] WPIDS  
 DOC. NO. CPI: C1989-068509  
 TITLE: Novel DNA, plasmid and polypeptide(s) - useful as

anticarcinogenic agents.

DERWENT CLASS: B04 D16  
 PATENT ASSIGNEE(S): (SENG-I) SEN G  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 01095784	A	19890413	(198921)*		17
JP 08017716	B2	19960228	(199613)		15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 01095784	A	JP 1987-252174	19871006
JP 08017716	B2	JP 1987-252174	19871006

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 08017716	B2 Based on	JP 01095784

PRIORITY APPLN. INFO: JP 1987-252174 19871006

AB JP 01095784 A UPAB: 19930923

DNA having the following amino acid sequences, plasmids contg. the DNA, polypeptides contg. the amino acid sequences, a method for preparing said polypeptides and anticarcinogenic agents comprising the polypeptides are all new.

Met-Val-Arg-Ser-X-Thr-Arg-Thr-Pro Ser-Arg-Lys-pre -Val-Ala-His-Val -Val- which is amino acid sequences of the fourth exon of TNF (where X is Ser or Cys).

In an example, from THP-1 cells, mRNA were extracted by centrifugation and ethanol pptn.. By utilising the mRNA, cDNA libraries were formed by Cubler method and Okayama-Barg method. Screening of desired cDNA was conducted by making the obtd. cDNA libraries grow, converting plasmid DNA of double chains to that of single chain, hybridising the cDNA with DNA probes and detecting positive clones by autoradiography. Genome DNA were prep'd. by cultivating THP-1 cells, forming a suspension contg. the cells, and collecting the DNA by means of centrifugation, alcohol pptn., density gradient method and dialysing. Genome DNA fragments were collected by nick-translation, hybridisation and condensation of specific DNA, fragments. Genome libraries were formed by preparing **chimera** circular DNA and introducing the **chimera** DNA into E.coli RRI. (7) Xhol/PstI fragments were inserted into pUC540 to form pUC540 (TNF)x/p. Also Xhol-PstI fragments were digested and the obtd. HincII-PstI fragment, DheI-HincII fragments were synthesised, combined with either chain of a double DNA and inserted into BamHI-PstI site of pUC540 (TNF)x/p.

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